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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/077,137	02/15/2002	Browning Jeffrey	A080 US	2907
22852	7590	02/14/2006	EXAMINER	
FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP 901 NEW YORK AVENUE, NW WASHINGTON, DC 20001-4413			DUFFY, PATRICIA ANN	
			ART UNIT	PAPER NUMBER
			1645	

DATE MAILED: 02/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/077,137

Applicant(s)

JEFFREY ET AL.

Examiner

Patricia A. Duffy

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 7-20-05
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 4, 7-11, 15, 19-21, 25-52 is/are pending in the application.
- 4a) Of the above claim(s) 1, 4, 7-11, 15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 9-21, 25-52 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 2005
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

RESPONSE TO AMENDMENT

The response and amendment filed 7-20-05 has been entered into the record. Claims 2, 3, 5, 6, 12-14, 16-18, 22-24 have been cancelled. Claims 1, 4, 7-11, 15, 19-21, 25-52 are pending. Claims 19-21 and 25-52 are under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Priority

Applicants argue that they are entitled to the priority of 60/149,378 filed August 17, 1999 in view of page 2, lines 4-8, page 5, lines 1-14, page 6, lines 1-11, page 7, lines 15-31, page 8, lines 1-18, page 10, lines 8-19, page 11, lines 14-30 and parts of pages 14, 15 and 16. It is noted that the cited lines of page 5 do not provide support for pharmaceutical compositions that inhibit immunoglobulin expression, but immunoglobulin production. Page 5 provides for specific examples of a single fragment and IgGFc fusion not commensurate with the claimed invention. Page 7 does not provide for percent identity to the claimed fragments 1-51, 8-41 and does not support variants thereof. Page 8 recites percent identity to SEQ ID NO: 1 and not fragments thereof. Page 10 does not support B cell expression or expression of immunoglobulins. It merely supports B-cell maturation and secretion of immunoglobulin. Expression of immunoglobulin is inherent to B cells. B cells are in part defined by the cell surface IgD. It is these cells that mature into Ig secreting plasma B cells. As such, maturation and secretion of immunoglobulin does not support the ill-defined expression of B-cells and expression of immunoglobulin and one of skill in the art would not equate these parameters. Applicants also point to page 10 of the provisional document. The generic concept of fragments in general does not support the explicitly claimed fragment 1-51 or the claimed "fragments of fragments". Further, it does not support variants of these claimed fragments or fragments of the variable fragments. Page 14 describes analogs of SEQ ID NO: 1 in general and not the claimed fragments. Further,

its does not describe structural variants of SEQ ID NO: 1 that maintain functionality. Pages 15-16 provide for general methods of use and particular pharmaceutical compositions. For the foregoing reasons, the priority to the provisional document is denied. In order to be accorded the filing date of a provisional document under 119(e), the document must comply with 35 USC 112, first paragraph. The priority document does not describe the now claimed invention for reasons set forth above. The priority document does not comply with the enablement requirement of 35 USC 112, first paragraph because it does not enable the use of any pharmaceutical composition for any of the contemplated methods. The priority document fails to enable the claimed pharmaceutical compositions in that it does not demonstrate any of the requisite activities in vitro that would provide a nexus for in vivo activity. Further, the provisional document fails to demonstrate any activity in vivo.

Election/Restrictions

This application contains claims 1, 4, 7-11 and 15 drawn to an invention nonelected with traverse in the response filed 12-17-04. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Information Disclosure Statement

The information disclosure statement 7-20-05 has been considered and an initialed copy is enclosed.

Objections/Rejections Withdrawn

The objection to the oath or declaration is withdrawn in view of a copy of the originally filed MacKay declaration.

Claims 19-31 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 106, 107, and 151 of copending Application No. 10/380,703 are withdrawn in view of the amendment to claim 19 to insert structure.

The rejection of claims 19-31 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention in the Office Action mailed 3-17-05 is withdrawn in view of Applicants amendments to the claims.

The rejection of claims 19-21 under 35 U.S.C. 102(b) as being clearly anticipated by Bram et al (US Patent No 5,969,102, issued October 19, 1999) is withdrawn based on the amendments to the claims.

Objections/Rejections Maintained

The objection to claim 19 and all dependent claims is maintained. BCMA and BAFF are not defined in the independent claims under examination.

Claims 19, 27-34, 36-37, 39-41, 43-44, 46-48 and 50-51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection is maintained for reasons made of record for claims 19, 20, 21, 23, 24, 26, 27-31 in the office Action mailed 3-17-05.

The are directed to encompass corresponding sequences from other species, mutated sequences, allelic variants, splice variants, sequences that have a recited degree of identity (similarity, homology), and fragments thereof residues 1-51 of SEQ ID NO: 1 that bind BAFF and so forth. None of these sequences meet the written description

provision of 35 USC 112, first paragraph for reasons made of record. The specification provides insufficient written description to support the genus encompassed by the claims. Binding to BAFF is insufficient because BAFF is not defined in the claims and applicants have not provided any description of structural variants that bind. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). With the exception of SEQ ID NO: 1 and particularly disclosed B cell activating factor binding fragments thereof and IgFc fusions thereof, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Furthermore, Bork et al, 2000, Skolnick et al 2000, Doerks et al, Smith et al 1997, Brenner 1999 and Bork et al 1996) teach that the art recognizes that function cannot be predicted from structure. As such the specification lacks written description for genus of BAFF binding polypeptides variants and fragments, one skilled in the art would not recognize that applicants had possession of the genus of claimed polypeptides for therapeutic use as instantly claimed. The specie and particularly disclosed fragments thereof specifically disclosed are not representative of the genus because the genus is highly variant and the art recognizes at the time of the invention that similar structure does not predict similar function.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Applicants argue routine experimentation. The amount of experimentation is not a consideration for written description, either Applicant was in possession of the genus or not. Since it was known in the art that structure does not predict function and Applicants have not provided a description of a single variant that meets the function, Applicants did not have possession of the claimed genus. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. Here the asserted potential method is screening to test for function, comparison with the art. It is noted that written description is present for the genus or not. In the instant case structure does not predict function and the presence of mere function does not place the genus in possession of the inventors, when the specification lacks description of variants having that function sufficient to allow the skilled artisan in the art at the time the invention was made to ascertain possession of the genus.

Applicants' amendments are insufficient to obviate this rejection. The specification as filed does not provide description of a representative number of variants and fragments thereof with identical function, sufficient to allow the skilled artisan to envision the functioning genus and envision possession of the genus as now claimed.

Claims 19-21 and 25-52 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition comprising an isolated B cell activating factor receptor (BAFF-R) of SEQ ID NO: 1 or a fragment comprising residues 1-51 of SEQ ID NO: 1 that binds B cell activating factor (BAFF), wherein the BAFF-R is optionally fused to the Fc region of an immunoglobulin it does not reasonably provide enablement for sequence variants, naturally occurring variants, allelic variants, mammalian homologues or percent variants thereof and fusions to an immunoglobulin per se. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for reasons made of record in the Office Action mailed 3-17-05.

Applicants' arguments have been carefully considered but are not persuasive. Applicants argue that the test for enablement is that there is no undue experimentation. This is not persuasive for reasons made of record. Applicants argue that Non-critical feature of the invention may be supported by a more general disclosure than those at the heart of the invention. This is not persuasive; the heart of the invention is that which is now claimed. The claims are critical features that speak to the heart of the invention and therefore cannot be supported by a general disclosure. In response to applicant's argument based upon the age of the references, contentions that the references are old are not impressive absent a showing that the art tried and failed to solve the same problem notwithstanding its presumed knowledge of the references. See *In re Wright*, 569 F.2d 1124, 193 USPQ 332 (CCPA 1977). Applicants argue that one skilled in the art would know what amino acids are conserved and that proteins are surprisingly tolerant of amino acid substitutions and cite Bowie et al (Science, 247:1306-1310, 1990). This is not persuasive because Bowie et al requires comparison of sequences to discover how a protein folds and how it performs its functions or determination of a particular structure of a polypeptide. None of such data is present in the specification to allow the skilled artisan to immediately envision substitutions that would function. The relationship between the peptide sequence of a protein/peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (see Ngo et al, for example). Furthermore, Bork et al, 2000, Skolnick et al 2000, Doerks et al 1998, Smith et al 1997, Brenner 1999 and Bork et al 1996) teach that the art recognizes that function cannot be predicted from structure. The specification provides an invitation to make and test to see if one could use. The specification lacks guidance as to what changes could be specifically made that would result in a polypeptide that function as claimed. Additionally, as was found in *Ex*

parte Hitzeman, 9 USPQ 2d 1821 (BAPI 1987), a single embodiment may provide broad enablement in cases involving predictable factors such as mechanical or electrical elements, but more will be required in cases that involve unpredictable factors such as most chemical reactions and physiological activity. The present invention is drawn to peptide pharmaceuticals and in unpredictable and complex, where one skilled in the art may not treat all possible autoimmune disorder and B cell proliferate disorders by administration of the variant peptides and fragments claimed herein. Further, there is no activity demonstrated for the peptide of residues 8-41 of SEQ ID NO: 1. The courts have held that the disclosure is insufficient when testing is necessary to determine the actual use or possible lack of use (*In re Kirk and Petrow* 153 USPQ 48 (CCPA 1967). Applicants' have no written description for any of these other desirable variant peptides and are not enabled for such and that applicants' are not entitled for dominance of further patentable inventions by claims that are insufficiently supported by the specification (*In re Fisher*, 166 USPQ 18, CCPA (1970)). The courts have held "... in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provide broad enablement in the sense that once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved." (*In re Fisher* 166 USPQ 18 (CCPA)). Applicants argue that even if a nonfunctional variant exists, it does not prove lack of enablement from a claim. This is not persuasive, the issue is that no variants have been described or tested for functionality. Applicants argue that it is routine to screen for functional variants and cite Kricka et al 1995. This is not persuasive, when one has demonstrated variants exist that function similarly screening might be routine. However, in the instant case no variants have been disclosed and the fragment 8-41 of SEQ ID NO:1 has not been shown to have the recited properties. The specification invites one skilled in the art to search for operative

variants, without any expectation of success because none have been described in the specification that function and the art supra indicates that at the time that the invention was made that function could not be predicted from structure. The specification does not teach what structures to align, what substitutions could be made and what substitutions are functional. The specification as filed, must provide written description of a representative number of functional embodiments to support a genus claim. In the instant case, the specification does not teach a single operative variant and since the peptides are very short, the impact of any single amino acid will be greater on the overall tertiary structure of the peptide. The specification does not teach which amino acid are important in binding BCMA or important in the function of inhibiting B cell expression or immunoglobulin expression. This is left to the skilled artisan to discover. Without such guidance, mere random substitution provides for unpredictable effects on function. Thus, Applicants have not provided sufficient guidance as to which of the amino acids may be changed in the claimed BCMA peptide and still maintain biological activity or structural specificity is unpredictable and the experimentation left to those skilled in the art is extensive and undue.

The rejection is maintained.

The rejection of claims 19-21, 26-52 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Gross et al (WO/00/40716, published 13 July 2000) is maintained for reasons made of record in the Office Action mailed 3-17-05.

Applicants' arguments have been carefully considered but are not persuasive. Applicants argue that they are entitled to the priority date of provisional application 60/149,378 filed August 17, 1999. This is not persuasive, the provisional document lacks written description for reasons made of record above and is not enabled for the claimed invention reasons made of record herein.

The rejection of claim 25 under 35 U.S.C. 102(a) as anticipated by Gross et al (WO/00/40716, published 13 July 2000) is maintained for reasons made of record in the Office Action mailed 3-17-05.

Applicants' arguments have been carefully considered but are not persuasive. Applicants argue that they are entitled to the priority date of provisional application 60/149,378 filed August 17, 1999. This is not persuasive, the provisional document lacks written description for reasons made of record above and is not enabled for the claimed invention reasons made of record herein.

Claims 19-21, 25-52 are rejected under 35 U.S.C. 102(e) as anticipated by Shu et al (U.S. Patent No. 6,475,987, issued November 5, 2000, filed May 5, 2000 with benefit of priority to May 1, 2000, provisional application 60/201,012).

Applicants' arguments have been carefully considered but are not persuasive. Applicants argue that they are entitled to the priority date of provisional application 60/149,378 filed August 17, 1999. This is not persuasive, the provisional document lacks written description for reasons made of record above and is not enabled for the claimed invention reasons made of record herein.

Claims 19-21 and 25-52 are rejected under 35 U.S.C. 102(e) as anticipated by Shu et al (U.S. Patent Application Publication 2003/0148445 A1, published August 7, 2003, with benefit of priority to May 1, 2000, provisional application 60/201,012).

Applicant's arguments have been carefully considered but are not persuasive. Applicants argue that they are entitled to the priority date of provisional application 60/149,378 filed August 17, 1999. This is not persuasive, the provisional document lacks written description for reasons made of record above and is not enabled for the claimed invention reasons made of record herein.

New Objections/Rejections Based on Amendment

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: The specification fails to provide support for the language inhibiting B cell expression or immunoglobulin expression. Applicants pointing to the specification by page best resolve this issue and line number where these limitations can be found.

Claims 19-21, 25-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

All the claims recite the parameter of inhibiting B cell expression. B cell expression of what? The specification and the claims neither define nor describe what expressed product is inhibited. As such, the skilled artisan cannot readily ascertain the metes and bounds of the pharmaceutical composition.

As to claims 32-38 are *prima facie* indefinite because the phrase the transmembrane domain of BCMA does not have antecedent basis in the claims. Therefore, the skilled artisan would not be readily apprised of the metes and bounds of the transmembrane domain of BCMA. Applicants are reminded that limitations found in the specification are not read into the claims to provide for clarity.

Claims 19-21, 25-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The claims now recite "an amount of a BCMA polypeptide effective to inhibit B cell expression or immunoglobulin expression". Support for "B cell expression" and "immunoglobulin expression" is not readily apparent in the specification as filed. The specification supports B-cell maturation and secretion of immunoglobulin. Expression of immunoglobulin is inherent to B cells. B cells are in part defined by the presence of cell surface IgD. It is these cells that mature into immunoglobulin secreting plasma B cells. As such, maturation and secretion of immunoglobulin does not support the now recited B-cell expression and expression of immunoglobulin and one of skill in the art would not equate these phrases.

As to claims 19, 32 and 46 now recite "fused to a heterologous amino acid sequence. The conception of fusion to the genus of heterologous amino acid sequences is not readily apparent in the written description of the specification as filed. While the specification specifically supports Fc-IgG and Ig or Fc-Ig in general, the specification as filed does not conceive of any generic heterologous fusion sequence in a pharmaceutical composition. For example, claims of a reissue application are drawn to new matter since they broadly recite genus of "carrier particles" which is not disclosed in original patent, which discloses only subgenus of "magnetic carrier particles" and species of "iron, ferrites, nickel, and cobalt" carrier particles. It is noted that entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977). In re East and Harmon (CCPA) 181 USPQ 716 (May 9, 1974). This issue is best resolved by Applicants pointing to the specification by page and line number where specific written description support can be found for the newly claimed limitation.

Status of Claims

Claims 19-21, 25-52 stand rejected. Claims 1, 4, 7-11 and 15 are withdrawn from consideration as drawn to non-elected inventions.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

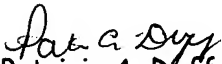
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can generally be reached on M-Th 6:30 am - 6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864.

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The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.


Patricia A. Duffy

Primary Examiner

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